Association of Blood Pressure Patterns with the Clinical Profile of Patients at St. Luke's Medical Center Quezon City

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Abstract

INTRODUCTION: Ambulatory blood pressure (BP) monitoring (ABPM) is useful for the assessment of hypertension and nighttime blood pressure (BP) patterns. This study aims to determine the prevalence of abnormal nocturnal BP patterns among Filipinos and its associated risk factors.

METHODS: This was a cross-sectional study of patients (n=304) who underwent ABPM. Age, sex, BMI (≥25 kg/m^2) hypertension, diabetes, smoking, lipid profile, creatinine, fasting glucose, previous MI and stroke were recorded. The degree of relationship of clinico-demographic factors with dipping and non-dipping BP patterns was determined.

RESULTS: Assessing for risk factors associated with abnormal nocturnal BP, only age (55 years, p=0.009) and diabetes (27.22%, p=0.038) were statistically significant. Age was a significant predictor of abnormal nocturnal BP, explaining 1.69% in the variation of nocturnal BP pattern (p=0.008). For every one-year increase in age, the odds of an abnormal nighttime BP pattern increase by approximately 2.5% (p=0.009).

CONCLUSION: There is a statistically significant association of age and diabetes with dipping and non-dipping BP patterns.

INTRODUCTION

Ambulatory blood pressure monitoring (ABPM) provides significant additional information over clinic monitoring of blood pressure (BP) among patients, and may be used to detect masked hypertension, loss of fall of nocturnal dip and nocturnal hypertension.[1] The association of ambulatory BP indices with major cardiovascular events is higher in hypertensive Asian patients than in the West.[2]

The evaluation of abnormal nocturnal BP patterns using ABPM provides prognostic and predictive value for future major cardiovascular events, stroke and end-organ damage.[3,4] Asleep systolic blood pressure (SBP) and its diminished nocturnal decline (normal nocturnal decline of 10% to 20%) is considered an important predictor of cardiovascular events, including morbidity and mortality.[3,5,6] Other nocturnal BP patterns include extreme dipping and reverse dipping. In extreme dipping, BP may fall markedly during sleep. In contrast, reverse dipping shows rising nocturnal BP, reaching levels higher than daytime levels. Among all the parameters of ABPM, nocturnal BP has the best overall reproducibility; hence, cardiovascular risk stratification may be more accurate if based on nocturnal BP levels.[7]

This study aimed to determine the clinical profile of dippers, non-dippers, extreme dippers and reverse dippers in patients who underwent ABPM at a tertiary medical center in the Philippines, and to identify risk factors and predictors for abnormal nocturnal BP patterns.

METHODS

This was a cross-sectional study that included all patients who underwent 24-hour ABPM at St. Luke's Medical Center Quezon City from January to December 2017 with complete clinical data, including laboratory results at most six months prior to the ABPM reading.

Patients records were retrieved and reviewed; demographic and clinical data were recorded, including age, sex, body mass index (BMI), diagnosis of hypertension, diabetes, smoking history, total cholesterol, low density lipoprotein, high density lipoprotein, triglycerides, creatinine fasting glucose, history of previous myocardial infarction and stroke.

In our institution, ABPM is performed by technicians of the Heart Institute using one of five standard ABPM machine (Oscar 2, Suntech Medical), which were calibrated monthly. The cuff is attached to the left upper arm, midway between the elbow and shoulder, and with the artery indicator over the patient's brachial artery, between the bicep and tricep muscles. Once turned on, the machine measures BP every 30 minutes over 24 hours. The ABPM results of all included patients were retrieved and examined. ABPM readings performed at other institutions were excluded. Nocturnal falls in SBP were calculated using the following formula: (awake SBP–sleep SBP)/awake SBP x 100.8 Those with a nocturnal fall in SBP of 10% to 20% were classified as dippers; 0% to <10% as non-dippers; >20% as extreme dippers; and <0% as reverse dippers.8 The nocturnal BP patterns of patients were then correlated with their demographic and clinical characteristics. No long-term follow-up was conducted.

All data were processed and encoded using Microsoft Excel. Frequencies and percentages were used to describe categorical variables, and mean and standard deviation for continuous variables. One-way ANOVA and Fisher's Exact test/ Chi squared test was used to analyze differences in means and frequency respectively. Crude and adjusted odds ratios and 95% confidence intervals were calculated using binary logistic regression to compare dippers against those with abnormal nocturnal BP (combined non-dippers, extreme dippers and reverse dippers). Null hypothesis was rejected at 0.05 α-level of significance. STATA 15.0 was used for data analysis.

Sample Size Calculation

Sample size was calculated based on the test of hypothesis for the difference between two proportions. It was assumed that hypertensive patients had a 35% prevalence of non-dipping while the prevalence of non-dipping in the general population was hypothesized to be 50% lower (i.e., 17.5%).8 Using an alpha error of 5%, power of 80-90% and a 1-tailed alternative hypothesis, the initial sample size calculated was 77–106 per group or 154–212 for two groups. Controlling for five more variables in the analysis with an additional 10% for each control variable, the final sample size required was 231–318.

Ethical Considerations

The clinical protocol and all relevant documents were reviewed and approved by the hospital's Institutional Ethics Review Committee. Patient confidentiality was maintained and anonymity of patient records was ensured by using a generated code for each record. The investigators were responsible for the integrity, accuracy and completeness of the study data.

RESULTS

Out of the 916 patients who underwent ABPM, 304 patients fulfilled the inclusion criteria and were included in the analysis. The mean age of included patients was 53.9 ± 12.7 years, with more females than males (57.6% vs 42.4%, respectively) and more patients with obesity compared to those without obesity (56.9% vs 43.1%, respectively). Classified by nocturnal BP patterns, 124 (40.8%) were dippers, 116 (38.2%) were non-dippers, 36 (11.8%) were extreme dippers, and 28 (9.2%) were reverse dippers. The age, sex distribution and BMI classification of were similar between groups.

Table 1. Demographic profile of patients who underwent 24-hr ambulatory BP monitoring

	Overall (n=304)	Dipper (n=124)	Non-Dippers (n=116)	Extreme dipper (n=36)	Reverse dipper (n=28)	p-value
	Mean ± SD; Frequency (%)					
Age, years	53.9 ± 12.7	51.6 ± 12.4	55.1 ± 12.6	56.2 ± 11.1	55.9 ± 15.2	0.099*
Sex						0.108†
Male	129 (42.4)	51 (41.13)	43 (37.07)	18 (50.0)	17 (60.7)	
Female	175 (57.6)	73 (58.87)	73 (62.9)	18 (50.0)	11 (39.3)	
BMI						0.368†
Obese	173 (56.9)	70 (56.5)	65 (56.0)	18 (50.0)	20 (71.4)	
Non-Obese	131 (43.1)	54 (43.6)	51 (44.0)	18 (50.0)	8 (28.6)	

**One-way ANOVA; †Chi-squared test*

Table 2 shows the clinical profile of the included patients. Majority of patients (71.7%) had hypertension and 23.0% had diabetes. Ten patients (3.3%) had a history of myocardial infarction and 16 (5.3%) had a history of stroke. There were no statistically significant differences in the clinical profiles of patients between the four groups.

Table 2. Clinical profile of patients who underwent 24-hr ambulatory BP monitoring

	Overall (n=304)	Dipper (n=124)	Non-Dippers (n=116)	Extreme dipper (n=36)	Reverse dipper (n=28)	p-value
	Frequency (%)					
Hypertension	218 (71.71)	82 (66.13)	91 (78.45)	24 (66.67)	21 (75)	0.165†
Diabetes	70 (23.03)	21 (16.94)	36 (31.03)	6 (16.67)	7 (25)	0.053†
Smoking history	15 (4.93)	8 (6.45)	4 (3.45)	2 (5.56)	1 (3.57)	0.736‡
MI history	10 (3.29)	4 (3.23)	3 (2.59)	1 (2.78)	2 (7.14)	0.597‡
History of stroke	16 (5.26)	6 (4.84)	7 (6.03)	1 (2.78)	2 (7.14)	0.827‡
Admission						0.114‡
Outpatient	302 (99.34)	124 (100)	115 (99.14)	36 (100)	27 (96.43)	
Inpatient	2 (0.66)	0 (0)	1 (0.86)	0 (0)	1 (3.57)	

†Chi-squared test; ‡Fisher's exact test

Table 3 shows the laboratory profile of patients and their nocturnal BP pattern. Majority of included patients had elevated low-density lipoprotein levels (68.4%) and low high-density lipoprotein (79.6%). There were no significant differences between the laboratory profile of patients between the four groups.

Table 3. Lipid profile, creatinine and fasting glucose of patients who underwent 24-hr ambulatory BP monitoring

	Overall (n=304)	Dipper (n=124)	Non-Dippers (n=116)	Extreme dipper (n=36)	Reverse dipper (n=28)	p-value
	Frequency (%)					
Total cholesterol						0.158†
Normal	185 (60.9)	69 (55.7)	77 (66.4)	19 (52.8)	20 (71.4)	
High	119 (39.1)	55 (44.4)	39 (33.6)	17 (47.2)	8 (28.6)	
LDL, mg/dL						0.484†
Normal	96 (31.6)	33 (26.6)	41 (35.3)	12 (33.3)	10 (35.7)	
High	208 (68.4)	91 (73.4)	75 (64.7)	24 (66.7)	18 (64.3)	
HDL, mg/dL						0.584†
Normal	62 (20.4)	30 (24.2)	20 (17.3)	7 (19.4)	5 (17.9)	
Abnormal	242 (79.6)	94 (75.8)	96 (82.8)	29 (80.6)	23 (82.1)	
Triglycerides						0.843†
Normal	228 (75.0)	94 (75.9)	87 (75.0)	25 (69.4)	22 (78.6)	
Abnormal	76 (25.0)	30 (24.2)	29 (25.0)	11 (30.6)	6 (21.4)	
Creatinine						0.442‡
Normal	274 (90.1)	111 (89.5)	107 (92.2)	30 (83.3)	26 (92.9)	
High	30 (9.9)	13 (10.5)	9 (7.8)	6 (16.7)	2 (7.1)	
Fasting glucose						0.569‡
Normal	272 (89.5)	113 (91.1)	104 (89.7)	30 (83.3)	25 (89.3)	
High	32 (10.5)	11 (8.9)	12 (10.4)	6 (16.7)	3 (10.7)	

†Chi-squared test; ‡Fisher's exact test

Table 4. Association of demographic and clinical factors to abnormal nocturnal BP

	Abnormal BP (n=180)	Normal (n=124)	Crude Odds Ratio (95% CI)	P-value
	Mean ± SD; Frequency (%)			
Age, years	55.5 ± 12.7	51.6 ± 12.4	1.025 (1.01 - 1.04)	**0.009**
Sex				
Male	78 (43.3)	51 (41.1)	Reference	-
Female	102 (56.7)	73 (58.9)	0.914 (0.57 - 1.45)	0.702
BMI				
Obese	103 (57.2)	70 (56.5)	1.032 (0.65 - 1.64)	0.894
Non-Obese	77 (42.8)	54 (43.6)	Reference	-
Hypertension	136 (75.6)	82 (66.1)	1.583 (0.96 - 2.62)	0.074
Diabetes	49 (27.2)	21 (16.9)	1.835 (1.03 - 3.25)	**0.038**
Smoking history	7 (3.9)	8 (6.5)	0.587 (0.21 - 1.66)	0.316
MI history	6 (3.3)	4 (3.2)	1.034 (0.29 - 3.74)	0.959
History of stroke	10 (5.6)	6 (4.8)	1.157 (0.41 - 3.27)	0.783
High cholesterol	64 (35.6)	55 (44.4)	0.692 (0.43 - 1.1)	0.123
High LDL	117 (65.0)	91 (73.4)	0.673 (0.41 - 1.11)	0.123
Abnormal HDL	148 (82.2)	94 (75.8)	1.476 (0.84 - 2.59)	0.174
Abnormal Triglycerides	46 (25.6)	30 (24.2)	1.076 (0.63 - 1.83)	0.788
High Creatinine	17 (9.4)	13 (10.5)	0.891 (0.42 - 1.91)	0.765
High Fasting glucose	21 (11.7)	11 (8.9)	1.357 (0.63 - 2.93)	0.436

Using binary logistic regression, the identified risk factors for abnormal nocturnal BP were age (crude OR 1.025; 95% CI 1.01–1.04; p=0.009) and diabetes (crude OR 1.835; 95% CI 1.03–3.25; p=0.038) (Table 4). Performing backward stepwise regression, age was identified as the only significant predictor for abnormal nocturnal BP. For every year older, the odds of an abnormal nocturnal BP pattern increase by approximately 2.5% (p=0.009), adjusting for sex, BMI, diabetes, and other co-variates. This model was statistically significant, explaining 1.69% in the variation of nocturnal blood pressure pattern (R^2=1.69%; p=0.008).

DISCUSSION

Our study showed that the prevalence of dippers was higher (40.7%) compared to non-dippers (38.2%). These rates were similar to those reported by Sales et al[4] but the rate of non-dippers was lower compared to studies done by Almelor et al (65.31%) and Pancho et al (53.85%).[9,10] However, all patients in these earlier studies had diagnosed hypertension. Verdecchia et al, on the other hand, revealed that the prevalence of non-dippers in essential hypertension was approximately 35%.[11] Similar findings were reported by Xu et al, where >50% were non-dippers, but this study was done in an inpatient setting.[12] Xu et al noted that stress could be a contributing factor to the higher rate of non-dippers in the clinical setting compared with the general population.

Age was identified as a predictor of abnormal nocturnal BP profile, where for every one-year increase in age, the odds of an abnormal nocturnal BP pattern increase by approximately 2.5% (p=0.009). O' Brien et al documented that non-dippers and reverse dippers were more frequent in the elderly and that physiologic nocturnal BP fall decreases after 60 to 70 years of age.[13]

Daytime naps are prevalent among the elderly in some societies and failure to account for daytime naps may lead to overdiagnosis of non-dippers. Asians are said to have less nocturnal BP fall compared to Caucasians and this discrepancy has sparked debate on the reproducibility of nocturnal BP; however, this variation may be partly due to daytime napping, wherein daytime napping may influence average daytime BP.[2] Hence, daytime napping should be taken into a consideration in studying nocturnal BP patterns.

It should also be emphasized that nocturnal BP patterns are closely associated with the quality of sleep and the elderly may have conditions that disturb sleep, such as prostatic hypertrophy, sleep apnea and sleep fragmentation. These factors may influence or even interfere with the prognostic value of nocturnal BP in the elderly.[13]

In this study, diabetes mellitus was a significant risk factor for abnormal nocturnal BP patterns. A non-dipper profile may reflect autonomic dysfunction or obstructive sleep apnea, which are often encountered in obese patients with diabetes.[13,14] In patients with diabetes, ABPM is more reproducible compared with office BP, and may reveal masked hypertension, which is present in around 50% of patients with diabetes.[13] However, definitive cut-off points for the diagnosis of hypertension based on ABPM measurements and therapeutic targets for diabetic patients are still undefined and are areas of ongoing research.[13]

Almost 12% of patients in this study were classified as extreme dippers. These patients are considered high risk for ischemic stroke and myocardial ischemia.[4] Possible factors that may contribute to extreme dipping include orthostatic hypotension, exaggerated morning BP surge, increased BP variability, increased arterial stiffness or injudicious use of BP-lowering treatment.[4]

Over 9% of patients in this study were reverse dippers. These patients are considered to have the worst prognosis among patients with abnormal nocturnal BP patterns. A meta-analysis that included 17,312 patients found that while extreme dippers and non-dippers had a 20% and 27% increased risk respectively, for total cardiovascular events, reverse dippers had a 79% increase.[7] Hence, careful attention should be accorded these patients, including a thorough evaluation of possible treatable causes, such as endocrine or renal disorders as well as obstructive sleep apnea.

Despite a growing number of studies, the pathophysiological mechanism underlying the worse cardiovascular outcomes in patients with abnormal nocturnal BP patterns remains unclear. While autonomic failure has been considered an important factor in the development of non-dipping patterns, some studies suggest that this alone is not a sufficient cause of abnormal nocturnal patterns.[15] Rest–activity patterns during the daytime, external day–night divergence in ambient light intensity and spectrum, as well as neuroendocrine, endothelial and hemodynamic factors also play important roles.[14] Nocturnal autonomic imbalance with sympathetic overactivity, altered baroreceptor sensitivity, propensity for myocardial repolarization, increased salt sensitivity or renal dysfunction with nocturnal volume overload are some of the hypothesized factors currently being investigated.[4,15]

The results of this study must be interpreted within the context of its potential limitations. The intake and adherence to antihypertensive medications and the class of antihypertensives received were not taken into account. In addition, the patients referred to this institution may not necessarily be representative of either the general or hypertensive population, and other co-morbidities such as cancer, obstructive sleep apnea, and neurologic and endocrine disorders that may affect the cardiometabolic profile of the subjects were not considered. Important variables such as physical activity and job stress were also not assessed. Furthermore, this was a cross-sectional study, where longitudinal data, such as serial changes in organ function or cardiovascular morbidity and mortality were all not assessed long term.

Future studies should consider patients' daily activities, such as daytime napping. Synchronization of blood pressure data to rest-activity cycle would help ensure the accuracy of the interpretation of ABPM findings. The intake of maintenance medications and

treatment adherence must also be considered in prospective studies. The role of morning BP surge evaluation using ABPM to prevent occurrence or recurrence of stroke may merit further investigation. Further studies of nocturnal blood pressure patterns in association with echocardiographic parameters, carotid intimal thickness and microalbuminuria may also be explored.

CONCLUSION

Significant associations were found between abnormal nocturnal BP patterns and age and diabetes mellitus. Age was identified as a predictor of abnormal nocturnal BP patterns. No significant association was found between nocturnal BP patterns and other clinical or laboratory factors investigated.

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